The Role of Autologous Platelet Rich Plasma in the Treatment of Osteoarthritis Knee

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ABSTRACT

Osteoarthritis represents failure of the joint where all the structures have suffered pathologic changes mainly hyaline cartilage degeneration. It is highly prevalent especially in old age group, and its ill impact on daily activities makes it a leading cause of disability in the older age group. To evaluate the effectiveness of autologous platelet rich plasma in treatment of osteoarthritis knee in reducing pain, stiffness and improving physical function and to find out the efficacy of platelet rich plasma in the treatment of osteoarthritis knee as a disease modifying, cost effective conservative modality. Total 60 patients were selected for the study fulfilling the inclusion criteria and were randomly divided into two groups of control (normal saline) and test (PRP) and were assessed using WOMAC scale and VAS scale for the assessment of pain stiffness and physical function, follow up was done at 6 weeks, 3 months and 6 months. The global WOMAC score (PRP) showed a mean of 73.3 at pre-injection period which decreased to 61.6 at 6 weeks follow up and 46.03 at 3 months follow up which reduced to 32.1 at 6 months. The mean pain score (PRP) reduced from 16.4 to 11.7 at 6 weeks post injection and 7.36 at 3 months post injection. At the end of 6 months follow up, mean pain score was found to be 5.5. The mean pain score in group 2 (control group) showed a marginal decrease from 16.2 to 13.9 at 6 weeks post injection but returned to 15.7 at 6 months follow up. Though the patients injected with normal saline as control group showed initial improvement with reduction of pain due to placebo effect, their symptoms reappeared after some time during the follow up. Thus we can conclude that autologous platelet rich plasma is an interesting modality for conservative treatment of osteoarthritis knee and has proved to be efficacious and cost effective measure in the observation period of six months..

Keywords:

autologous platelet, PRP, osteoarthritis knee

1. Introduction

Osteoarthritis represents failure of the joint where all the structures have suffered pathologic changes mainly hyaline cartilage degeneration. It is highly prevalent especially in old age group, and its ill impact on daily activities makes it a leading cause of disability in the older age group[1]. Because of ageing and obesity the prevalence of osteoarthritis is increasing.

Osteoarthritis involves certain joint and spares others. It commonly affects hip, knee, first metatarsophalangeal (MTP) joint and cervical and lumbosacral spine. In hands, distal and proximal interphalangeal joints and first carpometacarpal (CMC) are involved. Usually the wrist, elbow and ankle joints are not involved [2,3,4].

Diagnosis of osteoarthritis can be made by radiographic findings such as reduction of joint space and osteophytes, however most of the people with x-ray findings of osteoarthritis are asymptomatic. What concerns us is symptomatic osteoarthritis which includes joint pain, functional and vocational disability, visits to clinicians and disease cost.Pathological changes in osteoarthritis include hyaline cartilage loss, increase in thickness and sclerosis of subchondral bone, marginal osteophytes, meniscal degeneration. Various pathways lead to joint failure but the initial step is often joint injury due to failure of the protective mechanisms[5,6,7].

Osteoarthritis is different from simple wear and tear as its distribution is asymmetrical and is often associated with abnormal loading rather than frictional wear. Osteoarthritis is also associated with previous injury to the joint following any trauma and is called secondary osteoarthritis.Prevalence of primary osteoarthritis is 22-39% in India1 affecting mainly middle to old age group and is almost always associated with history revealing repetitive joint loading. However the metabolic derangements of articular cartilage were seen in a few patients[8,9,10].

2. Materials And Methods

STUDY DESING:Randomized control trial. Patients were assessed under parameters such as pain, stiffness, physical function using WOMAC scale and assessed for pain using visual analogue scale at pre-injection, 6 weeks post injection, 3 months post injection and 6 months post injection.

The patients attending the in-patient as well as the outpatient department of orthopaedics at Sri Lakshmi Narayana institute of medical sciences from September 2018 to august 2020 with complain of bilateral knee pain were screened and among those who were diagnosed with osteoarthritis knee were chosen for the study.

Selected patients were classified using the kellegren lawrance classification for osteoarthritis knee and were graded between grade 0 to grade 4 depending on the severity and were included in the study after informed written consent. Total of 60 patients were selected for the study and were randomly divided into two groups of 30 each. Group 1 received intra-articular injection of platelet rich plasma in bilateral knee and was considered as the study group. Group 2 received intra-articular normal saline and was considered as control group.

Randomization was done and both the groups were compared in relation to age ,gender, height, Body Mass Index and WOMAC score.Other parameters such as pain, stiffness and physical function were also compared pre as well as post injection.

Grade	Radiologic Findings
0	No radiological findings of osteoarthritis
Ι	Doubtful narrowing of joint space and possible osteophytic lipping
Π	Definite osteophytes and possible narrowing of joint space
III	Moderate multiple osteophytes, definite narrowing of joint space, small pseudocystic areas with sclerotic walls and possible deformity of bone contour
IV	Large osteophytes, marked narrowing of joint space, severe sclerosis and definite deformity of bone contour

Ahlback Radiological Crieteria

Grade of osteoarthritis	Description
Grade 0	No radiographic findings of osteoarthritis
Grade I	Joint space narrowing $< 3 \text{ mm}$
Grade II	Joint space obliterated or almost obliterated
Grade III	Minor bone attrition (< 5 mm)
Grade IV	Moderate bone attrition (5–15 mm)
Grade V	Severe bone attrition (> 15 mm)

3. Result And Discussion

Osteoarthritis is a clinically heterogenous degenerative condition which is characterized by articular cartilage destruction, due to failure of protective mechanisms and imbalance between cartilage degeneration and regeneration[11,12,13-17]. In our study we chose random 60 subjects with classical findings of osteoarthritis and randomly divided them into two groups of test subjects and control group respectively. Both these groups were compared on the baseline characteristics of age, height, weight, BMI, pre injection WOMAC score. 30 of these patients were given intra-articular platelet rich plasma and other 30 were given normal saline as control.





P value unpaired t test = 0.7798

Gender Distribution



P value chi squared test = 0.7953

Height Distribution



P value Unpaired t test = 0.7369





P value Unpaired t test = 1.0000



Bmi Distribution

P value Unpaired t test = 0.9368





Pain Score



Stiffness Score



Physical Function Score





The Efficacy of platelet rich plasma in reducing pain, stiffness and physical function were assessed and scored according to WOMAC scoring index for both study as well as control group. The results were analysed using unpaired t test and chi square test. Age distribution in group 1 (test group) showed mean age of 54.1 while group 2 (control group) mean age was 54.7. The p-value derived using unpaired t test was found to be 0.7798 rendering the age factor insignificant.

Gender distribution was compared in both groups and found to be 56.67 % in males and 43.3 % in females. The p-value using chi square test was found to be 0.7953. Thus the gender factor was insignificant. Height distribution in group 1 (test group) showed mean height to be 156.9 cm while group 2 (control group) mean height was found to be 157.5 cm. The p-value using unpaired t test was 0.7369 rendering the height factor insignificant.

Weight distribution in group 1 (test group) showed mean weight to be 66.2 kg while group 2 (control group) mean weight was found to be 66.2 kg. The p-value was found to be 1.0000. The weight factor was insignificant. BMI distribution in group 1 (test group) showed mean of 26.96 while the group 2 (control group) mean BMI was 26.9. The p-value was found to be 0.9368. The BMI was found to be insignificant.

Thus our study ensured that all the patients were comparable on baseline characters. The global WOMAC score showed a mean of 73.3 at pre-injection period which decreased to 61.6 at 6 weeks follow up and 46.03 at 3 months follow up which reduced to 32.1 at 6 months. Our study showed a significant decrease in global WOMAC score, which was also consistent throughout the study period. The individual variables such as pain, stiffness and physical function were assessed.

The mean pain score reduced from 16.4 to 11.7 at 6 weeks post injection and 7.36 at 3 months post injection. At the end of 6 months follow up, mean pain score was found to be 5.5

The mean pain score in group 2 (control group) showed a marginal decrease from 16.2 to 13.9 at 6 weeks post injection but returned to 15.7 at 6 months follow up. The p-value using unpaired t test showed significant improvement. Secondary variable stiffness showed significant difference at 3 month follow up and 6 month follow up. The mean physical function reduced from a pre injection score of 51.3 to s23.2 at 6 months follow up in group (test group).

Group 2 (test group) showed a marginal dip in mean physical function scores from 48.3 to 45.4 and to 43.6 at 3 months post injection. The score levelled to 46.1 at the end of 6 months. Visual analogue score showed a decrease in mean of 7.3 to 2.9 which denoted a change of patients

perception of pain from intense, dreadful, horrible pain to mild, annoying pain in group 1 (test group). Group 2 (control group) showed a marginal dip from 6.6 to 4.9 thus revealing insignificant changes in pain.

Thus there was significant reduction in pain in patients treated with autologous platelet rich plasma while the test group injected with normal saline initially showed reduction of pain due to placebo effect but ultimately resulted in return of pain and stiffness, thus showing that autologous platelet rich plasma is a superior entity in conservative treatment of osteoarthritis.

4. Conclusion

Osteoarthritis is a degenerative process lead to joint failure of a diarthrodial joint leading to destruction of articular cartilage due to failure of various protective mechanisms. The management of osteoarthritis varies from conservative methods like lifestyle modification, physiotherapy and surgical methods such as joint replacement arthroplasty depending on the stage of the disease [18-23].

The treatment of osteoarthritis ranges from conservative management with physiotherapy, non steroidal anti inflammatory medications, intra articular glucocorticoid injection, intra articular hyaluronic acid etc to arthroscopic management like debridement. Advanced cases of osteoarthritis where conservative management has failed to provide satisfactory results joint replacement arthroplasty is performed.

Pharmacological management of osteoarthritis with NSAIDs is associated with risk of gastrointestinal complications with an alarming rise in NSAIDs induced multisystem complications. Joint replacement arthroplasty is a definitive treatment but is reserved for advanced cases with failed conservative management, moreover the post operative morbidity, cost issues, need for technical expertise and revision prevents arthroplasty from being the most frequent form of treatment.

Autologous chondrocyte transplantation and attempts at cartilage repair using mesenchymal stem cells and autologous osteochondral plugs are currently under experimental stage. Autologous Platelet rich plasma serves as an entity to provide articular cartilage regeneration thus acting as a disease modifying method for osteoarthritis unlike other modalities of treatment which aim at halting the disease process. Platelet rich plasma offers beneficial effect of various growth factors in platelet to cause regeneration of the articular cartilage in a synovial joint.

In our study we injected a concentrated mixture of platelets in the joint cavity and observed the patients for reduction of pain, reduction of stiffness and improvement of physical function. Our study revealed a significant reduction of pain, stiffness and improvement of physical function in patients injected with autologous platelet rich plasma. Though the patients injected with normal saline as control group showed initial improvement with reduction of pain due to placebo effect, their symptoms reappeared after some time during the follow up.

Thus we can conclude that autologous platelet rich plasma is an interesting modality for conservative treatment of osteoarthritis knee and has proved to be efficacious and cost effective measure in the observation period of six months.

Funding: No funding sources **Ethical approval:** The study was approved by the Institutional Ethics Committee **Conflict Of Interest**

The authors declare no conflict of interest.

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References

- Pal CP, Singh P, Chaturvedi S, Pruthi KK, Vij A. Epidemiology of knee osteoarthritis in India and related factors. Indian J Orthop. 2016;50(5):518-522. doi:10.4103/0019-5413.189608
- [2] Ng NTM, Heesch KC, Brown WJ (2012) Strategies for managing osteoarthritis. Int J Behav Med 19:298–307
- [3] Xing D, Wang B, Zhang W, et al (2017) Intra-articular platelet-rich plasma injections for knee osteoarthritis: An overview of systematic reviews and risk of bias considerations. Int J Rheum Dis 20:1612–1630
- [4] Kanchanatawan W, Arirachakaran A, Chaijenkij K, et al (2016) Short-term outcomes of platelet-rich plasma injection for treatment of osteoarthritis of the knee. Knee Surgery, Sport Traumatol Arthrosc 24:1665–1677
- [5] Zhang W, Moskowitz RW, Nuki G, et al (2008) OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. Osteoarthr Cartil 16:137–162
- [6] Campbell KA, Saltzman BM, Mascarenhas R, et al (2015) Does intra-articular plateletrich plasma injection provide clinically superior outcomes compared with other therapies in the treatment of knee osteoarthritis? a systematic review of overlapping meta-analyses. Arthrosc J Arthrosc Relat Surg 31:2213–2221
- [7] Sundman EA, Cole BJ, Karas V, et al (2014) The anti-inflammatory and matrix restorative mechanisms of platelet-rich plasma in osteoarthritis. Am J Sports Med 42:35–41
- [8] van Buul GM, Koevoet WLM, Kops N, et al (2011) Platelet-rich plasma releasate inhibits inflammatory processes in osteoarthritic chondrocytes. Am J Sports Med 39:2362–2370
- [9] Chen X, Jones IA, Park C, Vangsness CT (2018) The efficacy of platelet-rich plasma on tendon and ligament healing: a systematic review and meta-analysis With Bias Assessment. Am J Sports Med 46:2020–2032
- [10] Kabiri A, Hashemibeni B, Pourazar A, et al (2014) Platelet-rich plasma application in chondrogenesis. Adv Biomed Res 3:138
- [11] Mifune Y, Matsumoto T, Takayama K, et al (2013) The effect of platelet-rich plasma on the regenerative therapy of muscle derived stem cells for articular cartilage repair. Osteoarthr Cartil 21:175–185
- [12] Dhillon MS, Patel S, John R (2017) PRP in OA knee update, current confusions and future options. Sicot-J 3:27
- [13] Andia I, Maffulli N (2013) Platelet-rich plasma for managing pain and inflammation in

osteoarthritis. Nat Rev Rheumatol 9:721-730

- [14]Filardo G, Di Matteo B, Di Martino A, et al (2015) Platelet-rich plasma intra-articular knee injections show no superiority versus viscosupplementation. Am J Sports Med 43:1575–1582
- [15]Bennell KL, Hunter DJ, Paterson KL (2017) Platelet-rich plasma for the management of hip and knee osteoarthritis. Curr Rheumatol Rep 19:24
- [16] Chang K-V, Hung C-Y, Aliwarga F, et al (2014) Comparative effectiveness of plateletrich plasma injections for treating knee joint cartilage degenerative pathology: a systematic review and meta-analysis. Arch Phys Med Rehabil 95:562–575
- [17] Huang P-H, Wang C-J, Chou W-Y, et al (2017) Short-term clinical results of intraarticular PRP injections for early osteoarthritis of the knee. Int J Surg 42:117–122
- [18] "The Use of PRP Injections in the Management of Knee Osteoarthritis." ukdiss.com. 11 2018.
- [19] Filardo G, Kon E, Di Martino A, et al (2012) Platelet-rich plasma vs hyaluronic acid to treat knee degenerative pathology: study design and preliminary results of a randomized controlled trial. BMC Musculoskelet Disord 13:229
- [20] Fernández-Cuadros, M.E.. (2018). Effectiveness of platelet-rich plasma (PRP) on pain, function and quality of life in knee osteoarthritis patients: a before-and-after study and review of the literature. MOJ Orthopedics & Rheumatology. 10. 10.15406/mojor.2018.10.00415.
- [21]Bliddal H, Leeds AR, Christensen R. Osteoarthritis, obesity and weight loss: evidence, hypotheses and horizons a scoping review. Obes Rev. 2014 Jul;15(7):578-86.
- [22]Görmeli, G., Görmeli, C.A., Ataoglu, B. et al. Multiple PRP injections are more effective than single injections and hyaluronic acid in knees with early osteoarthritis: a randomized, double-blind, placebo-controlled trial. Knee Surg Sports Traumatol Arthrosc 25, 958–965 (2017).
- [23]Gato-Calvo L, Magalhaes J, Ruiz-Romero C, Blanco FJ, Burguera EF. Platelet-rich plasma in osteoarthritis treatment: review of current evidence. Ther Adv Chronic Dis. 2019 Feb 19;10:2040622319825567.